

Poster presentation

## Statins cholesterol lowering and mental health: a review

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### Background

Epidemiological and clinical studies have suggested that powerful cholesterol lowering may have adverse effects on mood and psychological well-being. Reports in the early 1990s showed that LDL cholesterol lowering might have an undesirable impact on mental health (possible increase of violence, accidents and suicide). As a result, the scientific interest is strongly focused on the effects of statins therapy on mental status (i.e. irritability, depressive symptoms, and anxiety). The aim of our study is to review the literature involving statins and mental health and to analyze it by time.

### Materials and methods

Three medical libraries (MEDLINE, COCHRANE, ISI Web of Science) were systematically searched in order to investigate the cumulative randomized evidence on the possible existence of correlation between statin treatment and mental health. Three chronological periods were further defined for by-time analysis of medical literature: early 1990s, late 1990s and 2000s reports. We identified forty-five peer reviewed related reports and only seven related randomized studies.

### Results

In the early 1990s a meta-analysis raised concerns about a possible increase of deaths in groups receiving treatment for lowering serum cholesterol levels. This resulted in further investigation of the association between the reduction of cholesterol concentration and deaths or violent tendencies. In the late 1990s several double-blind ran-

domized trials showed that there is no statistically significant effect of low cholesterol concentrations on the psychological well-being. At present, a strong hypothesis has been put forward about the effect of the statins themselves on some specific psychological parameters. This effect seems to be unrelated to cholesterol levels. Many randomized controlled studies came to the conclusion that there is a reduction of depressive symptoms, anxiety and hostility in patients treated with statins. The lipophilic statins, as opposed to all other cholesterol-lowering drugs, appeared primarily responsible for the observed effect on psychological well-being. A cholesterol-independent immunomodulatory mechanism has been postulated. Penetration of the blood-brain-barrier by the lipophilic molecule results in: inhibition of HMG-CoA reductase, suppression of the Th1-type cytokines, interferon-gamma (IFN- $\gamma$ ) and interleukins IL-2 and IL-12; promotion of the secretion of Th-2-type cytokines and IL-4 and IL-5 and IL-10; lowering of tryptophan availability and decreasing of serotonin levels. Whether statins improve tryptophan metabolism is worth being tested in more clinical trials.

### Discussion

At present, statins are supposed to improve the psychological well-being and to reduce depressive symptoms, despite the early 1990s observations that statin treatment might be a risk factor for self-destructive behaviour even suicide. Individuals with current statin use may have a lower risk of developing depression, an effect that could be also explained by improved quality of life due to the

decreased risk of cardiovascular events or higher health consciousness in patients receiving long-term treatment. It seems to be possible that an independent immunoregulatory statin effect is responsible for the alteration of the psychological well-being in treated patients. Further laboratory and clinical research, additional to meta-analysis of the existed randomised trials would be useful.

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